Case presentation

By

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- A 65 y female
- A month history of progressive weakness, numbness of lower limbs and unsteady gait.
- loss of bowel and bladder control.
- On the day of presentation she was suddenly unable to stand from sitting position.
- intermittent history of fever but no weight loss, or night sweat, headache, vomiting and no seizure activity.
- No history of recent infections.

Examination:

- Conscious, alert and oriented.
- Temp. 38.0 °C, H.R 123, B.P 155/80 mmHg and R.R18 with 98% O2.
- CN: unremarkable.
- Motor examination: hypotonia in the lower limbs with power of 0/5, absent reflexes and down going planter responses bilaterally.
- There was loss of all sensation up to the nipples at the level of T4.
- Upper limbs: unremarkable.

- WBC 17.50×10^3/L, lymphopenia 11.6%, Hb 150 g/L,

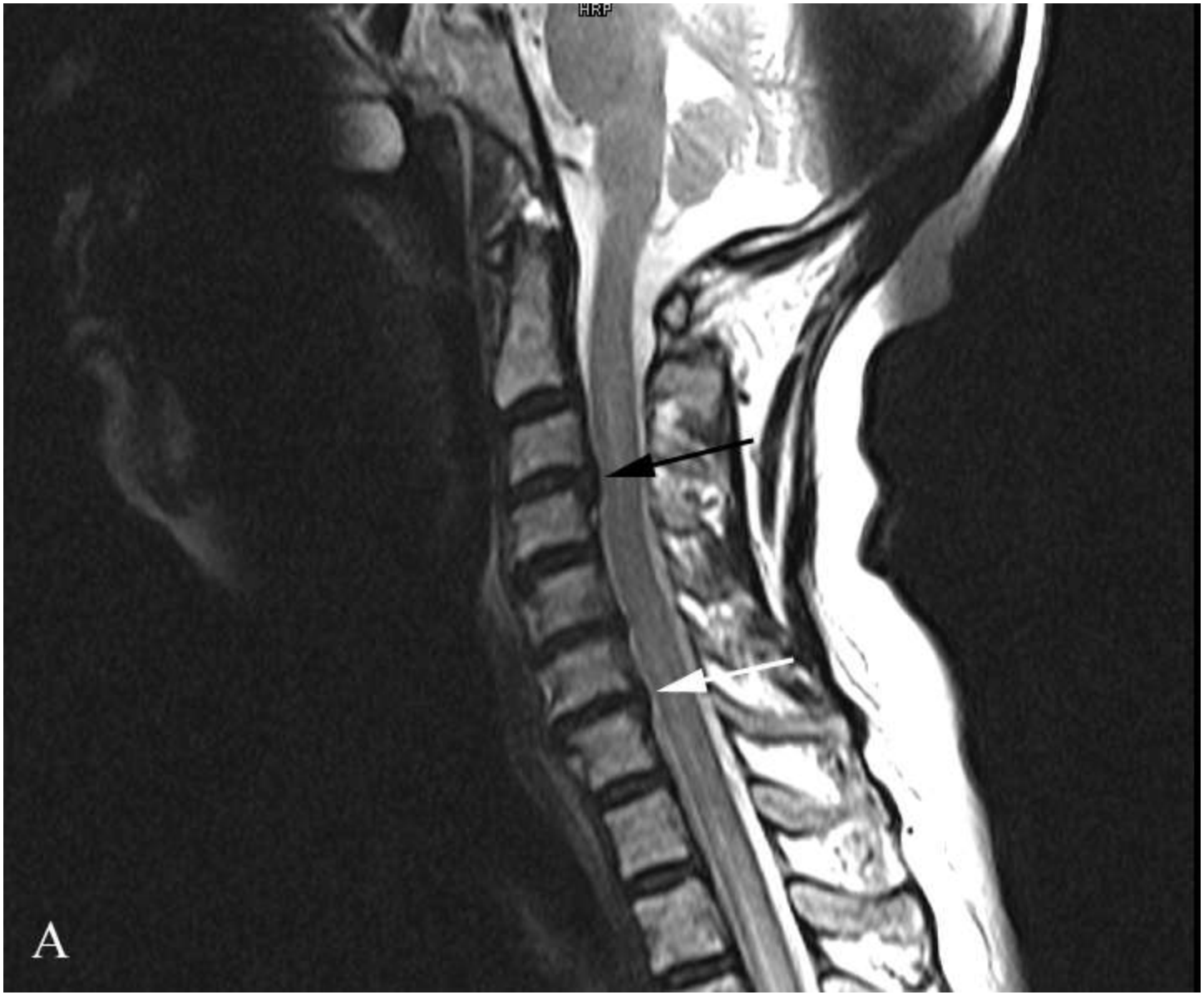
plat 203×103/L

- ESR:59.

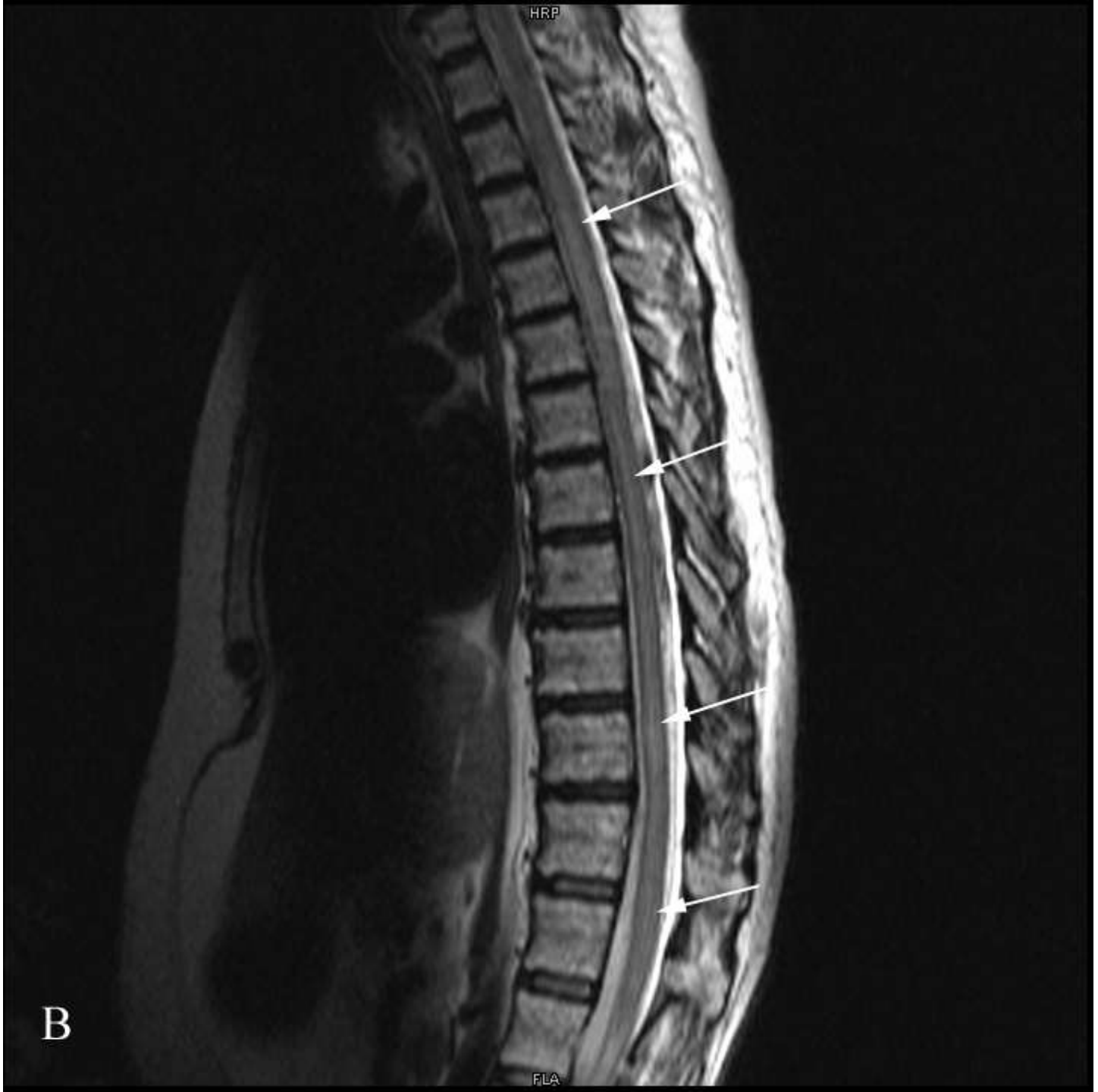
- CSF: WBC 371x10^6/L, 75% lymphocyte, glucose 5.5 mmol/L, protein1419 mg/L, negative cultures for all bacteria and viruses including acid fast bacilli with PCR technique.

- Urine culture: positive for E.coli.

- MRI & MRA:

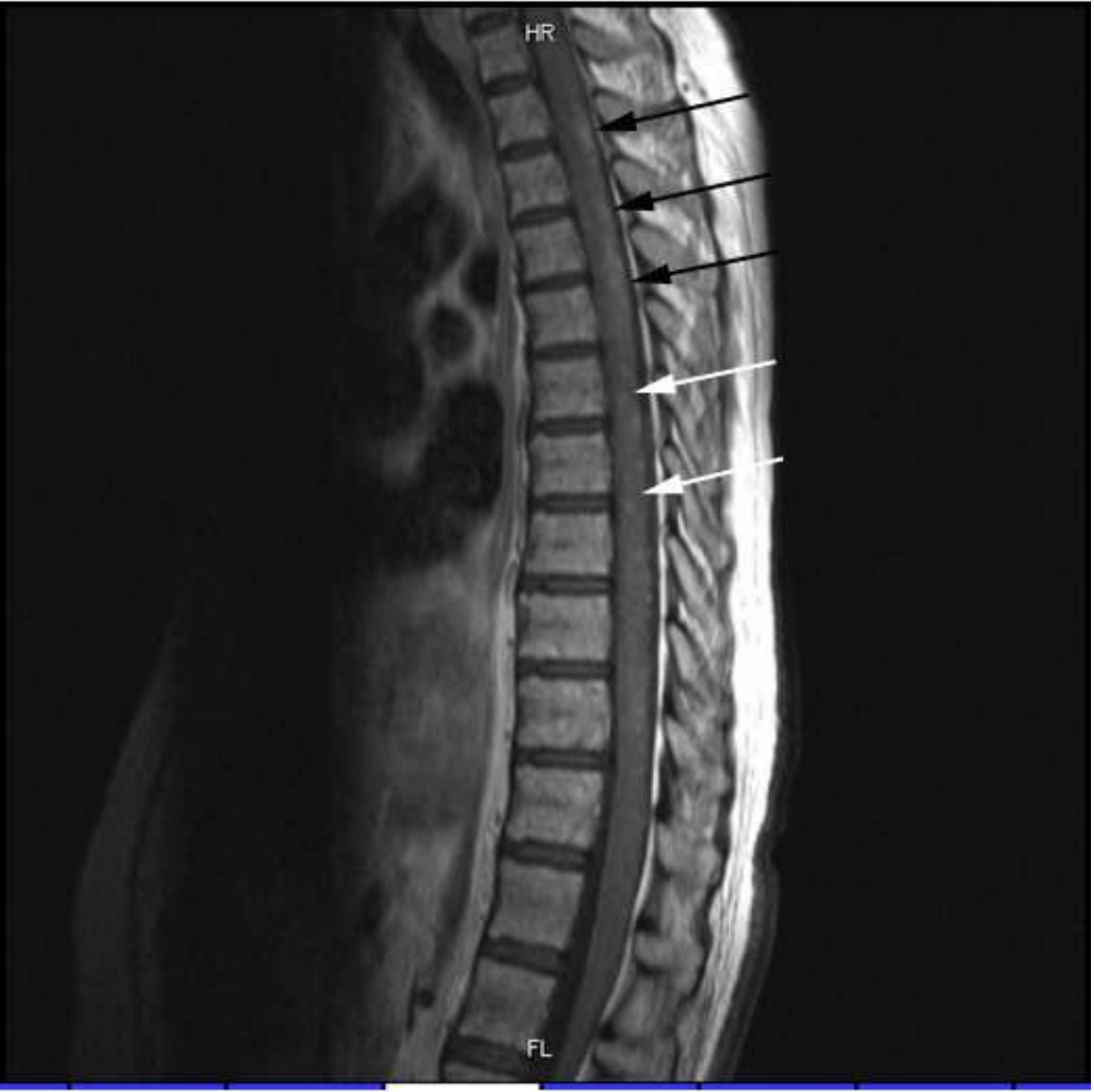


MRI of the cervical spine sagittal view, T2 weighted scan showing; mild cord compression at the C3-4 level (black arrow), the C6-7 level demonstrates a small disc centrally (white arrow). Hyperintensity is observed within the cord.


HRP
B
FLA

- Lupus anticoagulant: positive.
- IV pulse: methylprednisolone (MP) (1gram) X 5 days and IV ceftriaxone.
- Power 0/5 to 3/5 in lower limbs.
- The CSF analysis showed normal protein of 363mg/L, glucose of 3.4 mmol/L and WBC of 272x106/L with mainly lymphocytes.
- 2/52 power 0/5 again!

- The repeat MRI:



MRI of the thoracic spine sagittal view T1 weighted post gadolinium image showing some multifocal areas of enhancement within the cord. It predominantly involves the posterior aspect of the cord (black arrows). There are also extensive focal small enhancing lesions (white arrows).

Case presentation

- The suspicion of tuberculous myelitis was raised and the patient was started on anti-tuberculous medication

Case presentation

Rheumatology consultation:

- no joints pains, no morning stiffness

- O/E: butterfly rash sparing the nasolabial fold. No synovitis.
- ANA 1:320.
- Anti-ds DNA positive repeatedly at 32.9IU/ml (normal less than 10 IU/ml).
- The repeated lupus anticoagulant: positive again.

- *Transverse Myelitis as a presenting manifestation of SLE with aPL.*

Case presentation

- Another pulse IV MP (1 gm)X 5 days.
- All anti-TB meds were D/C.
- No additional therapeutic interventions.
- Her weakness improved significantly.
- Medications: hydroxychloroquine, a tapering regimen of oral prednisone, alendronate, oral calcium and vitamin D.
- Her power is almost 5/5 in proximal pelvic girdle muscles with normal sensory exam.
- The repeat MRI demonstrated some improvement in previously present hyperintensity within the upper thoracic cord.

كلمات في وسطية الإسلام

مازلت أؤكد أن العمل الصعب هو تغيير الشعوب، أما تغيير الحكومات فإنه يقع تلقائيًا عندما تريد الشعوب ذلك.

الشيخ محمد الغزالي

(1917 - 1996) أحد أبرز دعاة الفكر الإسلامي في العصر الحديث، عرف عنه محاربته للتشدد، وتسببت انتقاداته المتكررة للأنظمة الحاكمة العديد من المشاكل أثناء اقامته في مصر وفي السعودية.

Discussion

Late-onset SLE

- Late onset disease is the type of SLE whose manifestations begin after the age of 50 in majority of studies or after the age of 65.

- Rovensky, J. and Tuchynova, A., Systemic lupus erythematosus in the elderly. Autoimmun Rev, 2008. 7(3): p. 235-9.
- Karoubi Nordon, E., Hayem, G., Mentres, F., Palazzo, E., Legrain, S., Meyer, O., et al., Letter to the Editor: Late onset systemic lupus erythematosus: A new approach. Lupus, 2007. 16(12): p. 1011-4.
- Boddaert, J., Huong, D.L., Amoura, Z., Wechsler, B., Godeau, P., and Piette, J.C., Late-onset systemic lupus erythematosus: a personal series of 47 patients and pooled analysis of 714 cases in the literature. Medicine (Baltimore), 2004. 83(6): p. 348-59.
- Pu, S.J., Luo, S.F., Wu, Y.J., Cheng, H.S., and Ho, H.H., The clinical features and prognosis of lupus with disease onset at age 65 and older. Lupus, 2000. 9(2): p. 96-100.

Late-onset SLE

- The incidence of late-onset SLE is rare.
- As low as 3.7%* and to as high as 20.1%**.
- This may be related to the different ethnic backgrounds included in the studies and the variable definitions of late-onset SLE.

* Costallat, L.T. and Coimbra, A.M., Systemic lupus erythematosus: clinical and laboratory aspects related to age at disease onset. Clin Exp Rheumatol, 1994. 12(6): p. 603-7.

** Jacobsen, S., Petersen, J., Ullman, S., Junker, P., Voss, A., Rasmussen, J.M., et al., A multicentre study of 513 Danish patients with systemic lupus erythematosus. I. Disease manifestations and analyses of clinical subsets. Clin Rheumatol, 1998. 17(6): p. 468-77.

Late-onset SLE

- The sex ratio declines with age in SLE.
- In a pooled analysis of 714 cases of late-onset SLE reported in the literature and 4700 young SLE patients, the female to male ratio observed with age in SLE was 4.4:1 vs. 10.6:1 respectively*.
- This probably reflects the relationship between SLE and estrogen status which decline in the elderly.

Boddaert, J., Huong, D.L., Amoura, Z., Wechsler, B., Godeau, P., and Piette, J.C., Late-onset systemic lupus erythematosus: a personal series of 47 patients and pooled analysis of 714 cases in the literature. Medicine (Baltimore), 2004. 83(6): p. 348-59.

Late-onset SLE

- In general, late onset SLE is characterized by a lower disease activity.
- Skin manifestations, photosensitivity, Raynaud phenomenon, arthritis, nephritis and NP manifestations were less frequent in comparison with young SLE patients.
- In late-onset SLE, a higher occurrence of pulmonary involvement, serositis, and Sjögren's syndrome were observed.

- Boddaert, J., Huong, D.L., Amoura, Z., Wechsler, B., Godeau, P., and Piette, J.C., Late-onset systemic lupus erythematosus: a personal series of 47 patients and pooled analysis of 714 cases in the literature. Medicine (Baltimore), 2004. 83(6): p. 348-59.
- Costallat, L.T. and Coimbra, A.M., Systemic lupus erythematosus: clinical and laboratory aspects related to age at disease onset. Clin Exp Rheumatol, 1994. 12(6): p. 603-7.
- Rovensky, J. and Tuchynova, A., Systemic lupus erythematosus in the elderly. Autoimmun Rev, 2008. 7(3): p. 235-9.

Late-onset SLE

- Anti Ds DNA did not correlate with organ complications of late-onset disease in one study.
- A higher prevalence of rheumatoid factor, anti-Ro and anti-La antibodies were observed in late-onset SLE.
- However, lower prevalence of anti-RNP antibodies and hypocomplementemia were observed as well.

- Padovan, M., Govoni, M., Castellino, G., Rizzo, N., Fotinidi, M., and Trotta, F., Late onset systemic lupus erythematosus: no substantial differences using different cut-off ages. Rheumatol Int, 2007. 27(8): p. 735-41.
- Maddison, P.J., Systemic lupus erythematosus in the elderly. J Rheumatol Suppl, 1987. 14 Suppl 13: p. 182-7.
- Belostocki, K.B. and Paget, S.A., Inflammatory rheumatologic disorders in the elderly. Unusual presentations, altered outlooks. Postgrad Med, 2002. 111(4): p. 72-4, 77-8, 81-3.

Transverse Myelitis (TM)

- The American College of Rheumatology recognizes 19 SLE neuropsychiatric (NP) syndromes including myelopathy.
- The prevalence of TM in SLE patients is 1-2%.
- It can occur as the initial manifestation of SLE in up to 39% or within the first five years of a diagnosis of SLE in 42% of the total patient population analyzed in one study.
- The predominant presentation of TM in SLE is a sensory level commonly in the thoracic region, spastic paraparesis and sphincter disturbance consistent with the findings in our case.

- Nived, O., Sturfelt, G., Liang, M.H., and De Pablo, P., The ACR nomenclature for CNS lupus revisited. Lupus, 2003. 12(12): p. 872-6.
- D'Cruz, D.P., Mellor-Pita, S., Joven, B., Sanna, G., Allanson, J., Taylor, J., et al., Transverse myelitis as the first manifestation of systemic lupus erythematosus or lupus-like disease: good functional outcome and relevance of antiphospholipid antibodies. J Rheumatol, 2004. 31(2): p. 280-5.
- Kovacs, B., Lafferty, T.L., Brent, L.H., and DeHoratius, R.J., Transverse myelopathy in systemic lupus erythematosus: an analysis of 14 cases and review of the literature. Ann Rheum Dis, 2000. 59(2): p. 120-4.

MRI and Neuropsychiatric SLE

- MRI is considered the gold standard for the evaluation of central nervous system (CNS) manifestation of SLE in clinical practice.
- MRI finding are diverse, and atrophy and hyperintense white matter lesions often correlated poorly with clinical manifestations.
- It is more likely to show abnormalities if there are focal neurological deficits.

- Appenzeller, S., Pike, G.B., and Clarke, A.E., Magnetic Resonance Imaging in the Evaluation of Central Nervous System Manifestations in Systemic Lupus Erythematosus. Clin Rev Allergy Immunol, 2007.

- Only few cases of TM with longitudinal involvement of the spinal cord similar to that in which we described were reported in the literature.

- Chen, H.C., Lai, J.H., Juan, C.J., Kuo, S.Y., Chen, C.H., and Chang, D.M., Longitudinal myelitis as an initial manifestation of systemic lupus erythematosus. Am J Med Sci, 2004. 327(2): p. 105-8.
- Heinlein, A.C. and Gertner, E., Marked inflammation in catastrophic longitudinal myelitis associated with systemic lupus erythematosus. Lupus, 2007. 16(10): p. 823-6.
- Kimura, K.Y., Seino, Y., Hirayama, Y., Aramaki, T., Yamaguchi, H., Amano, H., et al., Systemic lupus erythematosus related transverse myelitis presenting longitudinal involvement of the spinal cord. Intern Med, 2002. 41(2): p. 156-60.

Antiphospholipid antibodies and TM

- The majority of TM cases reported in the literature were positive for aPL, 73% in one series and 55-64% in another.
- One of the strongest risk factors for the development of significant NP damage was the presence of aPL.
- Hanly, J.G. and Harrison, M.J., Management of neuropsychiatric lupus. Best Pract Res Clin Rheumatol, 2005. 19(5): p. 799-821.
- This has resulted in the introduction of anticoagulant therapy in the management of TM patients with positive aPL, but it remains controversial.

CSF in TM

- CSF: variable, for the majority cell count may be entirely normal (D'Cruz, D.P., et al J Rheumatol, 2004. 31(2)). or it may reveal lymphocytosis (D'Cruz, D.P., et al J Rheumatol, 2004. 31(2)). (Chen, H.C., et al Am J Med Sci, 2004. 327(2)) similar to our case or even neutrophilic predominate mimicking bacterial meningitis (Heinlein, A.C., et al Lupus, 2007. 16(10))

- Protein may be high or normal and glucose may be normal or low.

- Oligoclonal bands may also present (D'Cruz, D.P., et al J Rheumatol, 2004. 31(2)).

TM: a major therapeutic challenge!

- The ideal drugs, doses, and the length of treatment are not yet well defined.
- As TM in SLE is a rare manifestation treatment guidelines for this entity have not been developed.
- In older studies, most patients were treated with IV corticosteroid alone, whereas more recently some centers prefer a more aggressive approach with IV MP pulse therapy plus IV cyclophosphamide.

TM: a major therapeutic challenge!

- There were no clear differences between both drugs in five cases of TM when both were studied against each other after an induction therapy with MP.
- Barile-Fabris, L., Ariza-Andraca, R., Olguin-Ortega, L., Jara, L.J., Fraga-Mouret, A., Miranda-Limon, J.M., et al., Controlled clinical trial of IV cyclophosphamide versus IV methylprednisolone in severe neurological manifestations in systemic lupus erythematosus. Ann Rheum Dis, 2005. 64(4): p. 620-5

- However, several studies reported good to fair functional outcomes with combined treatment
- D'Cruz, D.P., Mellor-Pita, S., Joven, B., Sanna, G., Allanson, J., Taylor, J., et al., Transverse myelitis as the first manifestation of systemic lupus.

TM: a major therapeutic challenge!

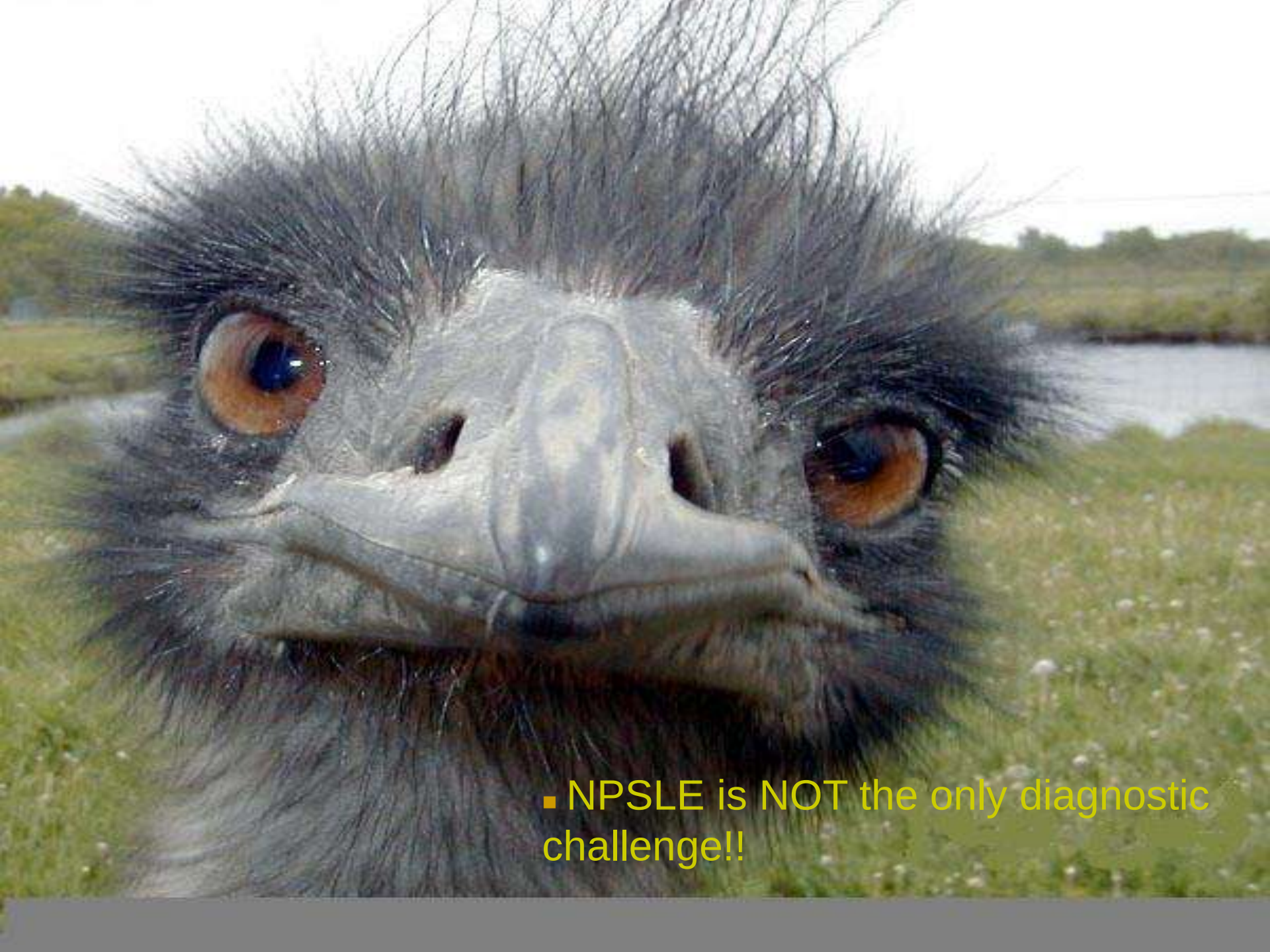
- Plasmapheresis has been used to complement this treatment regimen and it is still unclear if it has any additional therapeutic benefit.
- There are recent reports on the successful use of anti-CD20 in patients with TM
  - Chehab, G., Sander, O., Fischer-Betz, R., and Schneider, M., [Anti-CD20 therapy for inducing and maintaining remission in refractory systemic lupus erythematosus]. Z Rheumatol, 2007. 66(4): p. 328, 330-6.
  - Armstrong, D.J., McCarron, M.T., and Wright, G.D., SLE-associated transverse myelitis successfully treated with Rituximab (anti-CD20 monoclonal antibody). Rheumatol Int, 2006. 26(8): p. 771-2. [22, 23].
- The patient had significant improvement with the use of steroid.
- TM in the elderly might be controlled with the use of large dose of steroid only.

Take home message

- Late-onset SLE: >50, low disease activity, 4:1.
- TM presents with sensory level commonly in the thoracic region, spastic paraparesis and sphincter disturbance.
- TM can be a presenting feature of late-onset SLE.
- TM in late-onset SLE might be responsive to steroid therapy alone

A different challenge!

- NPSLE may still present a very difficult diagnostic challenge.
- Joseph, F.G., Lammie, G.A., and Scolding, N.J., CNS lupus: a study of 41 patients. Neurology, 2007. 69(7): p. 644-54.


NPSLE is NOT the only diagnostic challenge!!

SLE: The Challenge Continues..!

SLE is a challenging disease..!!!

- Challenge of clinical presentation.
- Challenge of diagnosis.
- Challenge of treatment.
- Challenge of severe lupus: high mortality!

لو عَلِمَ الشهداء أنكم
ستُعطُون أصواتكم
لنفس أفراد النظام
الذى قتَلَهُم فى الميادين
لما منَحُوكم بدماءهم
حق التصويت من البداية